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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/785,090	02/25/2004	Yoshihiro Takami	249424US0	8516

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/785,090	TAKAMI, YOSHIHIRO	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 9-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-8 and 15-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/27/2006*; 2/25/2004
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Official translation of reference

By Jiang Dwyer et al.

DETAILED ACTION

Claims 4-8 as amended and new claims 15-20 (filed 4/27/2006) are under examination in the instant office action.

Claims 1-3 and 9-14 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected invention. Applicant timely traversed the restriction requirement in the reply filed on 8/11/2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Response to Arguments

Applicant's arguments filed 4/27/2006 have been fully considered but they are not persuasive for the reasons below.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 4-8 as amended and new claims 15-20 remain/are rejected under 35 U.S.C. 102(b) as being anticipated by US 4,399,123 (Oliver et al.).

Claims are directed to an acellular dermal matrix that is decellularized, consists essentially of a dermis fraction and retains normal dermal matrix structure. The acellular dermal matrix is obtained by separating dermis from epidermis and treating the separated dermis with

protease and surfactant simultaneously. Some claims are further drawn to the acellular dermal matrix derived from human or pig skin. Some claims are further drawn to the use of trypsin as protease, to the use of polyoxyethylene p-t-octylphenyl ether as surfactant, to treating the separated dermis for 3-5 hours at temperature 20-37°C.

US 4,399,123 (Oliver et al.) discloses an acellular dermal matrix made from human and from pig skin (examples 1 and 6). The dermis or the separated dermis is treated with enzymes including trypsin in saline and/or buffer solutions. The final product is purified so that all cellular elements are removed (col. 1, lines 59-61) and, thus, the final product of US 4,399,123 is "decellularized" or it does not contain cells as required for the claimed product. The final dermal matrix product of the cited patent contains only dermis fraction as disclosed. The final dermal matrix is described as "fibrious tissue" and, thus, it is a "normal" 3D collagen preparation. The final dermal matrix is said to provide for a "normal" skin appearance upon implantation (col. 5, lines 40-50) and, thus, it is characterized by "a normal dermal matrix structure" within the meaning of the claims and when read in the light of specification (page 14, lines 9-21). Therefore, the final products as disclosed and as claimed are characterized by identical structure and they are considered to be identical.

Furthermore, the product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. MPEP 2113. Although the cited patent does not disclose the use of polyoxyethylene p-t-octylphenyl ether as surfactant in combination with protease for treating the separated dermis, the final structure of the dermal matrix as disclosed by the cited patent appears to be the same as the claimed dermal matrix as explained above. Moreover, the same enzyme such as protease or trypsin is used for making acellular dermis that

essentially consists of protein collagen. Thus, whatever structural alterations would occur, these alterations would clearly be identical as result of using identical protease. The limitations of new claims 15 and 16 are related to separation of dermis and epidermis. The cited product is made from a separated dermis. Thus, the limitations of claims 15 and 16 do not appear to provide for a distinct structure of product. With respect to new claims 17-20 it is noted that although concentrations of reagents, time and temperature for treating dermal materials might affect the final product, however their impact would also depend, for example, on amounts of starting dermis and, thus, the final differences, if any, would not be determined.

Therefore, the final products as disclosed by US 4,399,123 (Oliver et al.) and as claimed are characterized by identical structure and they are considered to be identical.

With regard to the cited US 4,399,123 (Oliver et al.) applicant argues that the cited dermal matrix would be denatured as result of extended time periods of exposure to trypsin and, thus, the cited dermal matrix would not retain a "normal" dermal matrix structure (response page 9). At the very least this argument is not found convincing because the claimed term "normal" is broad and open to various interpretations. The cited US 4,399,123 (Oliver et al.) describes the final dermal matrix as a "fibrious tissue" and, thus, it is a "normal" 3D collagen-containing preparation. The cited final dermal matrix is said to provide for a "normal" skin appearance upon implantation (col. 5, lines 40-50) and, thus, it is characterized by "a normal dermal matrix structure" within the meaning of the claims and when read in the light of specification (page 14, lines 9-21). Therefore, the final products as disclosed and as claimed are characterized by identical structure and they are considered to be identical.

2. Claims 4, 6 and 7 as amended and new claims 15-20 remain/are rejected under 35 U.S.C. 102(b) as being anticipated by Takami et al. (IDS reference; Jpn. J. Burn. Inj. December 2000, Vol. 26, No. 5, pages 39-45).

Claims are directed to an acellular dermal matrix that is decellularized, consists essentially of a dermis fraction and retains normal dermal matrix structure. The acellular dermal matrix is obtained by separating dermis from epidermis and treating the separated dermis with protease and surfactant simultaneously. Some claims are further drawn to the acellular dermal matrix derived from human skin. Some claims are further drawn to the use of polyoxyethylene p-t-octylphenyl ether (same as Triton X-100, see specification page 12, line 17) as surfactant, to treating the separated dermis for 3-5 hours at temperature 20-37°C.

The reference by Takami et al. discloses an acellular dermal matrix made from human skin and decellularized by treatment with protease such as dispase and surfactant such as Triton X-100 (see entire document including abstract). The cited reference clearly states that the 3D collagen structure of dermal matrix was kept intact after dispase/Triton treatment (page 41, par. 2, last line). Thus, the final structure of cited dermal matrix is identical to the claimed product within the meaning of the claims and in the light of specification (page 14, line 10-20). Although the reference by Takami et al. does not clearly disclose separation of dermis from epidermis as step in making dermal matrix, the reference clearly teaches that the final dermal matrix is acellular. Thus, in the absence of cells in the final product as disclosed by Takami et al., the epidermis has been removed from dermis because epidermis mostly consists of layers of cells. Therefore, the cited reference anticipates the claimed invention.

With regard to the cited reference by Takami et al. applicant argues that the cited dermal matrix retains basement membrane and, thus, the final product is structurally different (response pages 10-11). Yet, claims are not limited to the exclusion of basement membrane and/or its components. Moreover, the present invention appears to employ at least some amounts and/or components of basement membrane as disclosed (page 14, lines 18-21). Furthermore, the cited reference describes that "a part of the basement membrane structure" remains in the final product (page 43, last 4 lines). Thus, the cited and the claimed acellular dermal matrices as claimed and as disclosed cannot be distinguished.

3. Claims 4-6 and 8 as amended and new claims 15-20 remain/are rejected under 35 U.S.C. 102(b) as being anticipated by Jiang Duyin et al. {Chinese Journal of Burns, (2002 Feb) 18 (1) 15-8}.

Claims are directed to an acellular dermal matrix that is decellularized, consists essentially of a dermis fraction and retains normal dermal matrix structure. The acellular dermal matrix is obtained by separating dermis from epidermis and treating the separated dermis with protease and surfactant simultaneously. Some claims are further drawn to the acellular dermal matrix derived from pig skin. Some claims are further drawn to the use of trypsin as protease, to the use of polyoxyethylene p-t-octylphenyl ether (same as Triton X-100, see specification page 12, line 17) as surfactant, to treating the separated dermis for 3-5 hours at temperature 20-37°C.

The reference by Jiang Duyin et al. discloses an acellular dermal matrix made from pig skin that is decellularized by treatment with trypsin and Triton X-100 (entire document including

English abstract, in particular). Thus, the cited reference clearly anticipates the claimed invention.

With regard to the cited reference by Jiang Duyin et al (2002) applicant argues that it does not disclose a detailed method of how all cellular components in the dermis are removed (response pages 11-12). However, the claimed invention is directed to a product not to a method of making.

Applicant also appears to argue that the cited dermal matrix retains some basement membrane (response page 12). Yet, claims are not limited to the exclusion of basement membrane and/or its components. Moreover, the as-filed specification discloses that the basement membrane component and/or the expression of type IV is attenuated or reduced (page 14, lines 18-21) and that at least some amounts and/or components of basement membrane remain in the final product (page 18, line 31). Thus, the cited and the claimed acellular dermal matrices as claimed and as disclosed cannot be distinguished.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4-8 as amended and new claims 15-20 remain/are rejected under 35 U.S.C. 103(a) as being unpatentable over Takami et al. (IDS reference; Jpn. J. Burn. Inj. December 2000, Vol.

26, No. 5, pages 39-45) and Jiang Duyin et al. {Chinese Journal of Burns, (2002 Feb) 18 (1) 15-8} taken with US 4,399,123 (Oliver et al.) and US 5,336,616 (Livesey et al.).

Claims are directed to an acellular dermal matrix that is decellularized, consists essentially of a dermis fraction and retains normal dermal matrix structure. The acellular dermal matrix is obtained by separating dermis from epidermis and treating the separated dermis with protease and surfactant simultaneously. Some claims are further drawn to the acellular dermal matrix derived from human or pig skin. Some claims are further drawn to the use of trypsin as protease, to the use of polyoxyethylene p-t-octylphenyl ether as surfactant, to treating the separated dermis for 3-5 hours at temperature 20-37°C.

The cited references by Takami et al. and by Jiang Duyin et al. are relied upon as explained above. They both teach an acellular dermal matrix that is decellularized by treatment with protease and surfactant. The same surfactant Triton X-100 is used for making both dermal matrices. The reference by Takami et al. teaches the use of dispase as protease for obtaining human dermal matrix. The reference by Jiang Duyin et al. teaches the use of trypsin as protease for obtaining pig dermal matrix.

Thus, the references are missing particular disclosure about human skin derived preparation of acellular dermal matrix that is decellularized with trypsin.

However, both dispase and trypsin are alternative or equivalent proteases that are used for obtaining acellular dermal matrices as taught by US 5,336,616 (col. 9, lines 53-56) and that are applicable for dermal matrix preparation derived from animal skin including human (col. 23, line 9). Furthermore, US 4,399,123 (Oliver et al.) demonstrates the use of trypsin for both human and

pig dermis derived preparations that are free of cells and cellular materials (col.4, lines 56-63 and examples 1 and 6).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to obtain human skin derived preparation of acellular dermal matrix that is treated with trypsin with a reasonable expectation of success in decellularizing human dermal matrix and reducing its antigenic properties as adequately taught and suggested by the cited references. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

With regard to the claims rejection under 35 USC § 103 applicant's main argument is based on the cited teaching by US 5,336,616 (Livesey et al.). Applicant appears to argue that the cited patent is nonanalogous art (response page 13).

In response to the applicant's argument that US 5,336,616 (Livesey et al.) is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, US 5,336,616 (Livesey et al.) clearly states that it relates to processing acellular collagen-based tissues matrix, for example: see abstract, first line. The instant claim 4 is directed to an acellular dermal matrix and the dermal matrix composed of collagen. Thus, the cited patent is clearly on

the same field of endeavor and pertinent to the particular problem with which the applicant was concerned.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

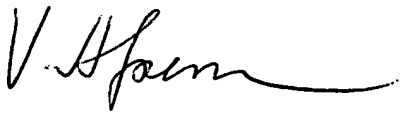
The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

July 6, 2006



VERA AFREMOVA

PRIMARY EXAMINER